IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMICUS THERAPEUTICS US, LLC and AMICUS THERAPEUTICS, INC.,	)	
Plaintiffs,	)	C.A. No. 22-1461 (CJB)
v.	)	CONSOLIDATED
TEVA PHARMACEUTICALS USA, INC. and TEVA PHARMACEUTICALS, INC,	)	
Defendants.	)	

AMICUS'S ANSWERING BRIEF IN OPPOSITION TO AUROBINDO'S MOTION FOR SUMMARY JUDGMENT OF INVALIDITY UNDER 35 U.S.C. § 101

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Amicus respectfully requests that the Court deny Aurobindo's summary judgment motion of invalidity under § 101 as to Asserted Claims[1] of U.S. Patent Nos. 11,633,388 ("'388 patent"), 12,042,489 ("'489 patent"), 12,042,490 ("'490 patent") (collectively, "Reassessment Mutations Patents"), and 11,833,164 ("'164 patent") ("Engineered Mutations Patent").

I. STATEMENT OF NATURE AND STAGE OF THE PROCEEDINGS

This case is set for a bench trial on September 29, 2025, and expert discovery is completed. D.I. 196; D.I. 213. In January 2025, Aurobindo requested permission to file a motion for summary judgment based only on "the plain language of the claims." D.I. 198 at 1. Aurobindo committed that it would support "any motion for summary judgment solely with precedent, the intrinsic record and testimony from Plaintiffs' own witnesses" and "if Aurobindo determines that expert opinion testimony is warranted to rebut Plaintiffs' expert(s) on issues relevant to § 101, Aurobindo will not file a motion for summary judgment." D.I. 198 at 2. The Court granted Aurobindo's request. D.I. 202. Aurobindo then filed the instant motion. D.I. 226.

II. SUMMARY OF THE ARGUMENT

Aurobindo's motion fails to analyze step one and step two of *Alice* separately as required by the law. D.I. 226 at 12–13. Even if it had, Aurobindo's arguments fail at both steps.

Step One. Contrary to Aurobindo's argument, the Asserted Claims are not directed to a natural phenomenon. Rather, they are directed to a specific method of treatment of specific patients using a specific compound. Each of the Asserted Claims requires a "method of treating Fabry disease, the method comprising administering migalastat to a patient in need thereof, wherein the patient" has a specific mutation. And nine of the ten Asserted Claims require a dosing regimen of 150 mg of migalastat hydrochloride (equivalent to 123 mg of the free base form of

[1] The Asserted Claims are claims 8 and 36 of the '388 patent, claims 17 and 23 of the '489 patent, claim 9 of the '490 patent, and claims 23–27 of the '164 patent.

migalastat) every other day for the treatment. *See* '338 patent cl. 36; '489 patent cl. 17, 23; '490 patent cl. 9; '164 patent cl. 23–27.

The Asserted Claims are what the Federal Circuit has called "typical" patent-eligible treatment claims "on a new use of an existing drug." *Nat. Alts. Int'l, Inc. v. Creative Compounds, LLC*, 918 F.3d 1338, 1345 (Fed. Cir. 2019). As the Federal Circuit "explained in *Vanda Pharmaceuticals Inc. v. West-Ward Pharmaceuticals International Ltd.*, 887 F.3d 1117, 1134–36 (Fed. Cir. 2018), claims that are directed to particular methods of treatment are patent eligible." *Id.* at 1344. There, the Federal Circuit reversed a judgment of ineligibility under § 101 where, as here, the claims require administration of a substance that alters the subject's natural state, because "[t]hese are treatment claims and as such they are patent eligible." *Id.*

That the claimed inventions of the Asserted Claims rely on the relationship between a genetic mutation's amenability to migalastat therapy and the successful treatment with migalastat of a patient having such mutation does not make them patent-ineligible, as Aurobindo asserts. The Asserted Claims teach specific methods of treatment of Fabry disease for specific patients using a specific compound based on that relationship; they are not claims directed to the relationship itself. And the claims require more than mere observation of that relationship: the claims "require[ ] a doctor to affirmatively administer a drug to alter a patient's condition from their natural state." *Id.* at 1344–45.

Such specific treatment claims—that "rely on the relationship between the administration of the drug and the physiological effects in the patient"—are patent eligible, as the Federal Circuit has repeatedly confirmed. *Id.* at 1345; *see id.* at 1346–47 (reversing district court judgment of patent-ineligibility under § 101 because the "Method Claims at issue are treatment claims."); *Endo Pharms. Inc. v. Teva Pharms. USA, Inc.*, 919 F.3d 1347, 1355 (Fed. Cir. 2019) (citation omitted)

(reversing district court judgment of patent-ineligibility under § 101 because claims are "'directed to a specific method of treatment for specific patients using a specific compound at specific doses to achieve a specific outcome.' Our precedent leaves no room for a different outcome.").

Step Two. Because Aurobindo's motion fails at step one of *Alice,* the Court can deny Aurobindo's motion without reaching step two. But even if the Court were to reach step two, Aurobindo fails to meet its burden because its motion does not adduce any facts as to whether the claim limitations here "involve more than the performance of 'well-understood, routine, [and] conventional activities previously known to the industry.'" *Berkheimer v. HP Inc.*, 881 F.3d 1360, 1367 (Fed. Cir. 2018). Indeed, Aurobindo does not recite this legal framework for step two in its motion, let alone address the highly factual question of what was well-understood, routine, and conventional as of the priority dates of the Asserted Patents.

This is deliberate: Aurobindo did not submit any expert opinions on this issue—or § 101 at all—and cannot do so now or at trial. And the reality is that the parties vigorously dispute the scope and content of the prior art which would inform the step two analysis, which is fatal to Aurobindo's motion. Amicus has submitted extensive expert testimony for the Reassessment Mutations Patents that, in May 2017, persons of ordinary skill in the art did not consider migalastat to be a well-understood, routine, and conventional treatment for patients having the mutations identified in the Asserted Claims of those patents. Amicus SOMF ¶¶ 9–11.[2] And for the Engineered Mutations Patent, Amicus has submitted extensive expert testimony that, in August 2019, physicians did not consider migalastat to be a well-understood, routine, and conventional

[2] Amicus has filed a Response to Aurobindo's Statement of Material Facts and also Amicus's own Concise Statement of Material Facts, referred to herein as "Amicus SOMF."

treatment for patients having the mutations identified in the Asserted Claims of that patent. *Id.* ¶ 12.

Aurobindo ignores these facts in its motion, and even if Aurobindo had addressed them, there would be material factual disputes fatal to Aurobindo's summary judgment motion.

III. STATEMENT OF FACTS

The Asserted Claims recite methods of treating patients who have certain genetic mutations causing their Fabry disease. Fabry disease is a rare lysosomal storage disease. *See* Ex. A (Hopkin Rebuttal Report) ¶¶ 43–44. Lysosomes are critical recycling centers within the body; enzymes within the lysosome help process and break down various substances that build up in cells such as the fatty globotriaosylceramide or "Gb3." *Id.* The enzyme that breaks down Gb3 is α-galactosidase A or "α-GAL A." *Id.* ¶ 43. Fabry patients have a mutation in the gene for α-GAL A such that the body is unable to make fully functional α-GAL A or any α-GAL A at all, and thus the body is unable to break down Gb3 and related substances. *Id.* ¶¶ 47–48. As a result, Gb3 and related substances can accumulate in the cells, which leads to organ damage, particularly in the kidneys and heart. *Id.* ¶ 44. Unlike many genetic disorders, there are thousands of different mutations in the α-GAL A gene that can lead to Fabry disease. *Id.* ¶ 48.

Until migalastat was approved by the United States Food and Drug Administration ("FDA") in August 2018, the only approved treatment for Fabry disease was enzyme replacement therapy ("ERT"), where a non-mutated form of α-GAL A is infused into a patient. *Id.* ¶¶ 401–02. However, ERT has a number of downsides, including generation of an anti-enzyme immune response, and inability for the replacement enzyme to penetrate the heart and kidney in sufficient amounts. *See* Ex. B (Jefferies Opening Report) ¶ 58. ERT also takes a substantial amount of time to administer because the infusion typically takes 1–2 hours and is administered every two weeks. *Id.* ¶ 59.

As an alternative to ERT, Amicus developed migalastat (Galafold®), which is a small molecule drug taken orally and dosed at 123 mg every other day (equivalent to 150 mg of migalastat hydrochloride). Ex. A (Hopkin Rebuttal Report) ¶¶ 51–53; Ex. C (Galafold Label). Migalastat is a molecular chaperone, meaning it stabilizes the patient's own genetically mutated α-GAL A rather than relying on infused α-GAL A replacement. Ex. A (Hopkin Rebuttal Report) ¶¶ 51–53. However, migalastat is not an effective treatment for all patients with Fabry disease because some α-GAL A mutations cannot be stabilized with migalastat. *Id.* ¶ 51. Indeed, the prior art taught that Fabry patients with certain mutations could ***not*** be treated with migalastat. *See id.* ¶¶ 101–02.

Prior to the Asserted Patents, it was not known which Fabry patients ***could*** be treated with migalastat and Amicus later proved that some mutations previously believed to be unresponsive to migalastat treatment are, in fact, amenable to migalastat treatment. *Id.* ¶¶ 54–56. Amicus spent years developing a test—called the Migalastat Amenability Assay or the Good Laboratory Practice ("GLP")-validated HEK assay described in some of the Asserted Patents—that could reliably predict clinical response to such treatment. *Id*. Using that assay, Amicus then was able to determine that Fabry patients with certain mutations could be treated with migalastat, specifically with 150 mg migalastat every other day, including patients with certain mutations that previously were thought to be untreatable with migalastat and patients with certain mutations where it was unknown whether they could be treated with migalastat. *Id.*

Amicus then applied for patents, claiming a method of treating Fabry disease for those patients using migalastat. Those are the Asserted Claims of the Reassessment Mutations Patents: claims 8 and 36 of the '388 patent, claims 17 and 23 of the '489 patent, and claim 9 of U.S. the '490 patent. Prior to the priority date of the Asserted Claims of the Reassessment Mutations

Patents (May 30, 2017), ERT was the only FDA-approved treatment for Fabry disease, and persons of ordinary skill in the art would not consider migalastat to be an appropriate treatment for patients having the mutations identified in the Reassessment Mutations Patent claims because, at the time, persons of ordinary skill in the art did not know that those mutations were amenable to migalastat treatment. *Id.* ¶¶ 402–05; Amicus SOMF ¶ 9–11.

Additionally, Amicus devoted resources to create new, previously unknown mutations to the α-GAL A gene that had not been associated with Fabry disease before, and determined that some of those engineered mutations can, in fact, be associated with Fabry disease and be treated with migalastat, specifically with 150 mg every other day, aiding in earlier diagnosis and treatment of Fabry patients with those mutations. Ex. A (Hopkin Rebuttal Report) ¶¶ 76–78. Amicus's Engineered Mutations Patent claims methods of treating Fabry patients having those mutations using migalastat. '164 patent cl. 23–27; Ex. A (Hopkin Rebuttal Report) ¶¶ 79–80. Likewise, prior to the priority date of the Asserted Claims of the Engineered Mutations Patent (August 7, 2019), ERT was still widely being used for the treatment of Fabry patients, and persons of ordinary skill in the art would not consider migalastat to be an appropriate treatment for patients having the mutations identified in the Asserted Claims of the Engineered Mutations Patent because, at the time, persons of ordinary skill in the art did not know that those mutations were amenable to migalastat treatment. *Id.* ¶¶ 412–14; Amicus SOMF ¶ 12.

IV. LEGAL STANDARD FOR SUMMARY JUDGMENT

Summary judgment requires Aurobindo to satisfy its burden of showing "that there is no genuine dispute as to any material fact and that the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a); *Ideal Dairy Farms, Inc. v. John Labatt, Ltd.*, 90 F.3d 737, 743 (3d Cir. 1996). In reviewing the record, "the court must draw all reasonable inferences in favor of the nonmoving party, and it may not make credibility determinations or weigh the evidence." *Reeves*

v. Sanderson Plumbing Prods., Inc., 530 U.S. 133, 150 (2000) (citation omitted). A dispute between the parties' experts can "raise genuine issues of material fact which must be resolved by a fact finder." *Cellectis S.A. v. Precision Biosciences, Inc.*, 937 F. Supp. 2d 474, 486 (D. Del. 2013).

The *Alice* step two inquiry involves factual determinations that may not be amenable to resolution on summary judgment. *See Berkheimer*, 881 F.3d at 1370 ("Whether claims 4–7 perform well-understood, routine, and conventional activities to a skilled artisan is a genuine issue of material fact making summary judgment inappropriate with respect to these claims.").

V. ARGUMENT

Invalidity under 35 U.S.C. § 101 is analyzed under the two-step analysis set forth in *Alice*. Under *Alice* step one, Aurobindo bears the burden of showing that "the claims at issue are directed to a patent-ineligible concept." *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. 208, 218 (2014). "*Alice* step one presents a legal question." *CardioNet LLC v. InfoBionic, Inc.*, 955 F.3d 1358, 1372 (Fed. Cir. 2020). If Aurobindo fails to satisfy its burden under step one, the Court can find the patent claims to be eligible under § 101, and deny Aurobindo's motion without reaching step two. *See Enfish, LLC v. Microsoft Corp.*, 822 F.3d 1327, 1339 (Fed. Cir. 2016) ("Because the claims are not directed to an abstract idea under step one of the *Alice* analysis, we do not need to proceed to step two of that analysis.").

To the extent reached, under *Alice* step two, Aurobindo bears the burden of showing that "the limitations of the claim apart from the law of nature," cannot "'transform the nature of the claim' into a patent-eligible application." *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 915 F.3d 743, 749 (Fed. Cir. 2019) (citation omitted). The claim is transformed when the additional "limitations 'involve more than the performance of well-understood, routine, [and] conventional activities previously known to the industry.'" *Berkheimer*, 881 F.3d at 1367.

"Whether something is well-understood, routine, and conventional to a skilled artisan at the time of the patent is a factual determination." *Id.* at 1369.

Aurobindo has not met its burden under either step of *Alice*.

A. *Alice* Step One: Aurobindo Fails to Show the Claims Are Directed to a Patent-Ineligible Concept

1. The Asserted Claims Recite Specific Methods of Treatment

Contrary to Aurobindo's argument that the Asserted Claims are directed to a natural phenomenon, the Asserted Claims require the administration of a specific compound migalastat as a specific method of treatment for specific patients with certain mutations that were identified based on the results of the Migalastat Amenability Assay referenced as the "GLP-HEK assay" in the patents. Aurobindo does not contest that the Asserted Claims recite methods of treatment (D.I. 226 at 3), which is evident from the plain language of the claims.

For example, claim 8 of the '388 patent recites a "method of treating Fabry disease."

> 1. A method of treating Fabry disease, the method comprising administering migalastat to a patient in need thereof, wherein the patient has an α-galactosidase A protein comprising a HEK assay amenable mutation selected from the group consisting of: A13P, A20D, Q57L, G80D, P146S, D175E, K213R, K213M, I242F, M267T, A309V, V316I, V316G, P323R, A352G, R356P, T385A, V390M, and G395A.
>
> 8. The method of claim 1, wherein the mutation is selected from the group consisting of: A13P, A20D, Q57L, G80D, P146S, D175E, K213M, I242F, M267T, A309V, V316I, V316G, P323R, A352G, R356P, T385A, V390M, and G395A.

Claim 1 also includes a specific administration step of the treatment: "administering migalastat to a patient in need thereof." The method further is only carried out on a subpopulation of patients having an identified mutation that is amenable to treatment from the results of the Migalastat Amenability Assay: "wherein the patient has an α-galactosidase A protein comprising a HEK assay amenable mutation selected from the group consisting of: A13P, A20D, Q57L, G80D, P146S,

D175E, K213M, I242F, M267T, A309V, V316I, V316G, P323R, A352G, R356P, T385A, V390M, and G395A." '388 patent, cl. 8. The Asserted Claims of the '489 and '490 patents recite the same limitations but identify specific patients with different mutations.

The Asserted Claims of the '164 patent recite a "a method for treatment of Fabry disease" with a specific administration step: "orally administering to the patient about 123 mg free base equivalent of migalastat or a salt thereof every other day."

> 23. A method for treatment of Fabry disease in a human patient in need thereof, the method comprising orally administering to the patient about 123 mg free base equivalent of migalastat or a salt thereof every other day, wherein the patient has an α-galactosidase A mutation selected from the group consisting of: Y184S, N228H, or T412I.

The method is also carried out on a subpopulation of patients having an identified genotype that is amenable to treatment from the results of the Migalastat Amenability Assay: "an α-galactosidase A mutation selected from the group consisting of: Y184S, N228H, or T412I." And nine of the ten Asserted Claims require a particular dosage regimen for the claimed treatment: '338 patent cl. 36 ("wherein the patient is administered about 150 mg of migalastat hydrochloride every other day"); '489 patent cl. 17, 23 (same); '490 patent cl. 9 (same); '164 patent cl. 24 (same); and '164 patent cls. 23, 25, 26, 27 ("administering to the patient about 123 mg free base equivalent of migalastat or a salt thereof every other day").

The patent specifications confirm that the claimed inventions are specific methods of treatment as to specific patients. For example, the patent titles describe the inventions as "methods of treating Fabry patients . . . " '388 patent at Title, '489 patent at Title, '490 patent at Title, and "methods of treating Fabry disease in patients having a mutation in the GLA gene," '164 patent at Title. The patent abstracts state, "[p]rovided are methods for treatment of Fabry disease in patients having HEK assay amenable mutations in α-galactosidase A," '388 patent at Abstract, '489 patent

at Abstract, '490 patent at Abstract, and "[p]rovided are methods of treating a patient diagnosed… with or suspected of having Fabry disease," '164 patent at Abstract.

2. Specific Methods of Treatment Are Patent Eligible

Aurobindo's motion fails at *Alice* step one because the Asserted Claims are specific method of treatment claims like the ones that the Federal Circuit has repeatedly determined are patent eligible. *See, e.g.*, *Vanda*, 887 F.3d at 1136 ("At bottom, the claims here are directed to a specific method of treatment . . . . Accordingly, the claims are patent eligible."); *Endo*, 919 F.3d at 1357 ("The claims in this case are directed to a new treatment for an ailment, albeit using a natural law or phenomenon. The claims are not directed to the ineligible subject matter itself and, as such, are eligible."); *Nat. Alts.*, 918 F.3d at 1344 ("The claims . . . require that an infringer actually administer the dosage formed claimed in the manner claimed, altering the athlete's physiology to provide the described benefits. These are treatment claims and as such they are patent eligible.").

First, in *Vanda*, the Federal Circuit held patent eligible claims "directed to a method of using iloperidone to treat schizophrenia" that required (i) performing a genetic test to determine whether a patient has a specific genotype and (ii) depending on the results of the genetic test, administering either less than 12 mg/day of iloperidone or between 12 mg/day and 24 mg/day. 887 F.3d at 1136. The Federal Circuit determined that, while the "inventors recognized the relationships between iloperidone" and the results of the genetic test (the same argument Aurobindo advances now), they properly "'claimed an application of that relationship' and not the relationship itself. *Id.* at 1135. The Federal Circuit reasoned that the claims were not directed to a natural relationship because the claims "recite the steps of carrying out a dosage regimen based on the results of genetic testing . . . These are treatment steps." *Id.* at 1135. The same is true here, where the Asserted Claims recite methods of treatment for a Fabry patient subpopulation with

specific mutations based on the results of the Migalastat Amenability Assay. *See, e.g.*, '388 patent cl. 8.

Second, in *Endo*, the Federal Circuit held that "the claims are directed to a patent-eligible method of using oxymorphone or a pharmaceutically acceptable salt thereof to treat pain in a renally impaired patient." 919 F.3d at 1353. The claims in *Endo* required first testing the level of renal impairment through an assay measuring the creatinine clearance rate and second, "giving a specific dose of the drug based on the results of kidney function testing." *Id.* at 1350, 1354. The Federal Circuit determined that while "the inventor here recognized the relationship between oxymorphone and patients with renal impairment [] that is not what he claimed. Rather, he claimed an application of that relationship—specifically, a method of treatment including specific steps to adjust or lower the oxymorphone dose for patients with renal impairment." *Id.* at 1354. Here too, the Asserted Claims are patent eligible as they claim an application of a relationship between mutation amenability and how a patient is likely to respond to migalastat, and teach administration of migalastat to only patients with certain genotypes. That the Asserted Claims do not require dose adjustment like in *Vanda* or *Endo* does not change patent eligibility, because the administration of migalastat itself is a still a "specific treatment step[]." *Id.* As in *Vanda*, that treatment step is based on the patients' genetic characteristics but the claims are not "directed to" those characteristics.

Third, in *Natural Alternatives,* the Federal Circuit held that the claims "are directed to patent eligible new ways of using an existing product, beta-alanine, they are treatment claims." 918 F.3d at 1345. The claims in *Natural Alternatives* recited "a method of increasing anaerobic working capacity" or "regulating hydronium ion concentrations in a human tissue comprising: providing an amount of beta-alanine to the blood or blood plasma *effective to increase*

beta-alanylhistidine dipeptide synthesis in the human tissue." *Id.* at 1343. The Federal Circuit determined that the claims were patent eligible because: "[a]dministering certain quantities of beta-alanine to a human subject alters that subject's natural state . . . and the subject's body will produce greater levels of creatine." *Id.* at 1344. And the court concluded that "[t]he claims not only embody this discovery, they require that an infringer actually administer the dosage form claimed in the manner claimed . . . . These are treatment claims and as such they are patent eligible." *Id.*

The same result is appropriate here, where the Asserted Claims require more than an observation of the relationship between a mutation's amenability under the Migalastat Amenability Assay and the likelihood of successful treatment of a Fabry patient. The Asserted Claims recite a step of administering migalastat based on the results of the Migalastat Amenability Assay. As in *Natural Alternatives*, this step shows the claim "require[s] specific steps be taken in order to bring about a change in a subject, altering the subject's natural state." *Id.* at 1345.

Aurobindo does not address *Natural Alternatives.* And *Aurobindo* incorrectly refers to *Vanda* and *Endo* as "decisions finding claims arguably directed to unpatentable subject matter as including that inventive step." D.I. 226 at 13. Those Federal Circuit decisions never reached step two of the *Alice* analysis, which sometimes is referred to as a "search for an 'inventive concept,'" *see Alice*, 573 U.S. at 217. That is because the *Vanda* and *Endo* claims were directed to patent-eligible methods of treatment at step one. Nor should the Court entertain Aurobindo's attempt to have the Court consider the novel aspects of the invention over the prior art at step one. It is well-established that this is legally improper as "[e]ligibility and novelty are separate inquiries." *Two-Way Media Ltd. v. Comcast Cable Commc'n, LLC*, 874 F.3d 1329, 1340 (Fed. Cir. 2017). And under step two, as discussed below, it was "not well-understood, routine, or conventional" to be

able to accurately identify which Fabry patients would be treatable with migalastat. Amicus SOMF ¶ 11–12, Ex. A (Hopkin Rebuttal Report) ¶ 406.

Aurobindo argues *Endo* is distinguishable because *Endo*'s claims were "directed to a multi-step process for treating pain in a renally impaired patient patent eligible." D.I. 226 at 13 (internal quotation marks removed).[3] This fails because patent eligibility does not turn on the number of steps in a claim or differences in specificity as to the claims. As the Federal Circuit determined in *Endo*, "any differences in specificity are not of a sufficient degree to convince us to conclude that the claims here should be ineligible as compared to the claims in *Vanda*." *Endo*, 919 F.3d at 1355. In so holding, the Federal Circuit rejected an argument that patent eligibility depends on the "precise methods" used to identify specific patients for treatment.

> Actavis argues that, unlike the *Vanda* claims, the '737 patent claims do not require that a biological sample be obtained or assayed in any particular way to determine the patient's creatinine-clearance rate. Appellee Br. 35 (citing *Vanda,* 887 F.3d at 1121). But this is a distinction without a difference. The court in *Vanda* reasoned that the claim was directed to "specific patients," without explicitly emphasizing the precise methods used to identify those specific patients.

Id. The Federal Circuit concluded that the claims there were patent eligible without holding (as Aurobindo now suggests) that the number of steps in the method is dispositive.

> At bottom, we conclude that the '737 patent claims are like those in *Vanda*. They are eligible because they are "directed to a specific method of treatment for specific patients using a specific compound at specific doses to achieve a specific outcome." *Id.* at 1136. Our precedent leaves no room for a different outcome.

Id.

Here, the Asserted Claims are patent eligible because they recite a method of treatment for specific patients (those with mutations identified as a result of the Migalastat Amenability Assay) using specific compound (migalastat) to achieve a specific outcome (to treat Fabry disease).

[3] Aurobindo incorrectly relies on the *Endo* district court decision reversed by the Federal Circuit rather than the Federal Circuit decision itself. D.I. 226 at 13.

Further, patent eligibility does not turn on the recitation in the claims of specific dosing. *Nat. Atls.*, 918 F.3d at 1346 (patent eligible claims did not recite specific dosing but "contain[ed] a dosage limitation by virtue of the 'effective' limitation" in that the "specification provides a method for calculating dosage based on a subject's weight"). In this case as in *Natural Alternatives,* the specification provides guidance as to the effective amount to administer *i.e.,* every other day of "about 100 mg to 150 mg free base equivalent (FBE)" of migalastat. *See, e.g.*, '388 patent at 3:16–22; '489 patent at 3:32–39; '490 patent at 3:32–39; *see also* '164 patent at 2:45–47 ("The method comprises administering to the patient a therapeutically effective dose of a pharmacological chaperone for α-Gal A . . . ."), 4:61–64 ("the dose of migalastat or salt thereof is from about 100 mg to about 150 mg free base equivalent (FBE)").

Finally, Aurobindo's reliance on *Mayo* is misplaced. Aurobindo argues that "the *Mayo* decision's determination that the method of optimization claims then before the Court were unpatentable applies equally to the Asserted Claims." D.I. 226 at 12. This fails because the Asserted Claims do not recite only an observation of the natural law as was the case in *Mayo*: the "claim in *Mayo* did not go beyond recognizing (i.e., 'indicates') a need to increase or decrease a dose" and "did not involve doctors *using* the natural relationship." *Vanda*, 887 F.3d at 1135. That is not the case here with the treatment claims at issue requiring administration of migalastat based on the results of the Migalastat Amenability Assay.

3. Aurobindo's Other Step One Arguments Fail

Aurobindo argues that a "genetic mutation's amenability to migalastat therapy is a natural phenomenon." D.I. 226 at 4. If this logic were correct, it would be true of every method of treatment: the way the human body responds to an administered drug is always governed by physiology. But just as in *Vanda*, where the genetic mutations in question affected how the body responded to the administered drug, this is in no way fatal to patentability. Amicus did not claim

the natural phenomenon of a particular mutation's amenability. Nor did Amicus claim a relationship between amenable mutations and migalastat. And Amicus did not claim the use of the diagnostic tool of the Migalastat Amenability Assay, a point that Aurobindo concedes. *See* D.I. 226 at 14 ("the Asserted Claims do not claim those assays"). Rather, Amicus claimed a method of treating an identified subpopulation of Fabry disease patients with migalastat. And Aurobindo cannot rewrite the claims to support its present motion.

Moreover, for Aurobindo to prevail on *Alice* step one, it is not sufficient to show that the claims use a natural phenomenon. "The 'directed to' inquiry … cannot simply ask whether the claims *involve* a patent-ineligible concept, because essentially every routinely patent-eligible claim involving physical products and actions *involves* a law of nature and/or natural phenomenon—after all, they take place in the physical world." *Enfish*, 822 F.3d at 1335; *see Endo*, 919 F.3d at 1354 ("[T]he inventor here recognized the relationship between oxymorphone and patients with renal impairment, but that is not what he claimed. Rather, he claimed an application of that relationship—specifically, a method of treatment including specific steps to adjust or lower the oxymorphone dose for patients with renal impairment.").[4]

B. *Alice* Step Two: Aurobindo Ignores the Factual Question of Whether the Claimed Invention Involves More Than the Performance of Well-Understood, Routine, and Conventional Activities, and Also Amicus's Material Facts

Aurobindo's motion should be denied for failing to satisfy *Alice* step one without reaching *Alice* step two. But even if the Court were to consider *Alice* step two, Aurobindo has failed to submit any evidence showing the Asserted Claims have no additional limitations that transform them into a patent-eligible application. Such transformation occurs when the additional limitations

[4] *Myriad*, *Athena*, and *Genetic Technologies* are inapposite. D.I. 226 at 12–13. The Asserted Claims are directed to methods of treatment, and they are not claims to the use of diagnostic method, to the genetic mutations themselves, or the recognition of a natural law.

"involve more than performance of 'well-understood, routine, [and] conventional activities previously known to the industry.'" *Berkheimer*, 881 F.3d at 1367. Because this is a question of fact, Aurobindo ignores it altogether and recites the legal standard for step two solely as a legal search for an inventive concept that requires no additional fact finding. D.I. 226 at 12. This is incorrect as a matter of law. In addition, Aurobindo has waived its ability to offer evidence at trial on step two because it did not disclose any expert opinions as to what was well-understood, routine, and conventional, let alone as to ineligibility under § 101. *See* Ex. D (Medin Opening Report) ¶¶ 12-13; Ex. E (Medin Rebuttal Report) ¶ 8; Ex. F (Medin Reply Report) ¶ 4–8. The only issues that are disputed for the bench trial are whether the Asserted Claims are invalid under § 103. *Id.*

But notwithstanding Aurobindo's representation to the Court that it would not rely on expert testimony in its motion [D.I. 198 at 2][5], it nonetheless asks the Court to consider what was known in the art prior to the Asserted Patents in the context of Aurobindo's incorrect interpretation of the claimed innovations. *See* D.I. 226 at 4 ("The Asserted Claims add to the '011 patent claims only by further describing Fabry patients actually in need of migalastat by reference to specific Fabry disease-causing genetic mutations determined to be amenable to migalastat."); D.I. 226 at 12 ("Unlike in *Mayo*, the Plaintiffs in this case do not claim any sort of improvement to any product or process."). Aurobindo's arguments are improper because patent "[e]ligibility and novelty are separate inquiries." *Two-Way Media*, 874 F.3d at 1340. But even if such arguments—contrary to Aurobindo's representation—were considered (they should not be), they only highlight the parties' many factual disputes as to what would have been known to a person of ordinary skill in the art and what would have been considered routine or conventional.

[5] In asking for leave to file its motion, Aurobindo represented that "Aurobindo commits to supporting any motion for summary judgment solely with precedent, the intrinsic record and testimony from Plaintiffs' own witnesses." D.I. 198 at 2.

What the prior art discloses is not intrinsic evidence, and is exactly the type of Hatch-Waxman inquiry that in Aurobindo's own words "concern[s] complex factual issues supported by competing experts perhaps oftentimes of similar credibility, rendering the Court's truth-finding task extremely difficult and, thus, benefitting from in-person testimony." D.I. 198 at 2. That is why district courts regularly deny summary judgment motions under § 101 because of factual disputes at step two. *See, e.g.*, *Prolitec Inc. v. Scentair Techs., LLC*, 770 F. Supp. 3d 730, 747 (D. Del. 2025) (denying summary judgment on *Alice* step two because "the dispute over whether the two-table aspect of the claimed invention was well understood, routine, and conventional requires resolution of a question of fact."); *Align Tech. Inc. v. 3Shape A/S*, No. 17-1646-LPS, 2020 WL 4926164, at *15 (D. Del. Aug. 14, 2020) ("the record concerning step two provides another basis to deny the motion for summary judgment" due to factual dispute as to what was "conventional, well-understood, or routine on the pertinent date").

In any event, Aurobindo's conclusory analysis as to step two does not meet its burden. Aurobindo asserts without support that there is no "material difference between the earlier-issued '011 patent claims and the recently issued Asserted Claims" other than that "the Asserted Claims further describe the Fabry patient(s) in need of migalastat, namely, and redundantly, those whose genetic mutations are determined to be migalastat amenable," and "identifying those mutations in a patent claim does not confer patentable characteristics to the claimed inventions." D.I. 226 at 2, 4. According to Aurobindo, the Asserted Claims "simply reclaim a previously patented method for treating Fabry disease and add adjectives to further describe the patient in need" and do not "describe any process or improvement to [Amicus's] previously claimed method of treating Fabry disease with 150 mg of migalastat." D.I. 226 at 12, 14. This fails.

Step two of *Alice* does not turn on whether the Asserted Claims are "reclaim[ing]" prior art (which they are not). As the Federal Circuit has explained, "[w]hether a particular technology is well-understood, routine, and conventional goes beyond what was simply known in the prior art. The mere fact that something is disclosed in a piece of prior art, for example, does not mean it was well-understood, routine, and conventional." *Berkheimer*, 881 F.3d at 1369; *see Bascom Glob. Internet Servs., Inc. v. AT&T Mobility LLC*, 827 F.3d 1341, 1350 (Fed. Cir. 2016) ("The inventive concept inquiry requires more than recognizing that each claim element, by itself, was known in the art."). Aurobindo also fails to separately analyze the Reassessment Mutations Patents and the Engineered Mutations Patent under *Alice* step two. Nor does Aurobindo identify a representative claim, let alone explain why it is representative. This is fatal to Aurobindo's motion because the Asserted Claims of the Reassessment Mutations Patents and the Engineered Mutations Patent have different priority dates. *See Scanner Techs. Corp. v. ICOS Vision Sys. Corp. N.V.*, 528 F.3d 1365, 1380 (Fed. Cir. 2008) (citation omitted) (noting the patent challenger must "prove invalidity by clear and convincing evidence, and that burden of proof never shifts to the patentee to prove validity").

Further, Amicus submitted voluminous material facts in expert discovery—that Aurobindo failed to rebut and ignores entirely in its motion—that would defeat summary judgment under *Alice* step two to the extent not resolved on step one. It was "not well-understood, routine, or conventional to be able to accurately identify which Fabry patients would be treatable with migalastat by the priority date of the Reassessment Mutations Patents." Amicus SOMF ¶ 11; Ex. A (Hopkin Rebuttal Report) ¶ 406. Specifically, Amicus's expert, Robert J. Hopkin, M.D., whose clinical research focuses on lysosomal storage diseases including Fabry disease, opined that "[i]t was not well-understood, routine, or conventional to use migalastat to treat Fabry disease patients

who have a mutation of the Reassessment Patent Claims by May 30, 2017." Amicus SOMF ¶ 9; Ex. A (Hopkin Rebuttal Report) ¶ 403. Because migalastat was not approved by FDA until August 2018, "[t]he only way Fabry patients would have been treated using migalastat, at the time, was in the clinical trials, and a person of ordinary skill in the art would not have considered such clinical trial treatments to be well-understood, routine, and conventional." Amicus SOMF ¶ 9; Ex. A (Hopkin Rebuttal Report) ¶ 405. For the Engineered Mutations Patent, Dr. Hopkin opined that in August 2019, even though there were some Fabry patients being treated with migalastat, "the Y148S, N228H, and T412I mutations were not previously associated with Fabry disease and a physician would have no reason to identify patients with those mutations as candidates for migalastat treatment," and, as a result, "[i]t was not well-understood, routine, or conventional to use migalastat to treat Fabry that had the α-Gal A mutations identified in the Asserted Claims of the Engineered Mutations Patent, i.e., Y184S, N228H, or T412I." Amicus SOMF ¶ 12; Ex. A (Hopkin Rebuttal Report) ¶¶ 411–14.

Aurobindo does not address let alone rebut these facts in its motion. And even if Aurobindo had addressed those facts, there would be material disputes precluding grant of summary judgment of invalidity under § 101 here.

VI. CONCLUSION

For the foregoing reasons, Amicus respectfully requests that the Court deny Aurobindo's motion. The Asserted Claims are patent eligible.

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July 3, 2025

CERTIFICATE OF SERVICE

I hereby certify that on July 3, 2025, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on July 3, 2025, upon the following in the manner indicated:

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